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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/933,548	08/20/2001	Christopher William Ogden	NORT 100	6550

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PATREA L. PABST
HOLLAND & KNIGHT LLP
SUITE 2000, ONE ATLANTIC CENTER
1201 WEST PEACHTREE STREET, N.E.
ATLANTA, GA 30309-3400

EXAMINER	
SAKELARIS, SALLY A	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/933,548	OGDEN ET AL.	
	Examiner	Art Unit	
	Sally A Sakelaris	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20, 23-34 and 36 -37* is/are pending in the application.

4a) Of the above claim(s) *10-14 and 17-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 15-16 with respect to nucleic acids* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *92002* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Arguments

Election/Restrictions

Applicant's election of Group I with traverse on 5/22/2003 is acknowledged as well as the cancellation of claim 38. Applicant should note that there further statement that "Applicants elect Pax 2 proteins as the species for the prosecution of the Groups II-X claims" is not understood by the examiner as these groups were not elected and neither was the protein embodiment of the invention. As such, this further election was not considered, as was not the embodiments involving a protein within the claims of 1-9 and 15-16, only the nucleic acid embodiment was examined in the elected group I of claims 1-9 and 15-16. Applicant's arguments filed 5/22/03 have been fully considered but they are not persuasive. The traversal is on the ground(s) that the office has "imposed the restriction on the basis that the claims are drawn to nucleic acids, proteins antibodies with no consideration of the relationships between the specific nucleic acids, proteins and antibodies defined in the claims"(Pg 9). The examiner maintains that each group is characterized by its distinct biomolecule, nucleic acid, protein, antibody etc, each being distinct as their composition is drastically different, ie nucleic acids are composed of nucleotides joined by phosphodiester linkages, while proteins are composed of sequential amino acids joined by peptide bonds. Applicant should also note, that method steps directed to, for example determining the susceptibility of a human patient to prostate cancer through nucleic acid detection as compared to through protein detection requires very different method steps and reagents because of their distinct compositions and varied applications. The Examiner reaffirms that the groups are properly separated as their inclusive products and

methods are comprised by different nucleic acids, proteins, and antibodies and as a result, create distinct inventions. The examiner maintains the restriction requirement made previously, as each group is correctly separated as unrelated or patentably distinct and the requirement is made final.

Objections to Specification and Figures

An objection is made to the specification and figures with respect to the Figure 5 series. Figure "5A3" follows Figure "5B" as "12/14" and "11/14" respectively in the figure section. An appropriate correction is required to correct the improper, non-consecutive listing of these figures, ie. "5A3" should precede "5B". Additionally, in the specification on page 56 of the figure descriptions, a "B1" and "B2" have been listed under "Figure 5A3" but no such subsections exist on the "5A3 figure" on the page "12/14". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-9 and 15-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following factors have been considered in formulating this rejection (*In re Wands,* 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the predictability or

unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Claims 1-9 and 15-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of diagnosing prostate cancer in a human patient comprising the steps of (i) obtaining a sample of the tissue, containing mRNA, in which prostate cancer is suspected or in which prostate cancer may be or has been found and (ii) detecting the presence or absence of mRNA expression which is associated with prostate cancer, does not reasonably provide enablement for (i), a method of determining the susceptibility of a human patient to prostate cancer or predicting the relative prospects of a particular outcome of prostate cancer predisposition by obtaining a sample containing only cells from tissues or a sample of urine, semen, blood, or lymphatic circulation, and (ii) determing whether the sample contains any level of any nucleic acid of Pax 2 associated with prostate cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 1-9 and 15-16 are broadly drawn to a method of determining the susceptibility of a human patient to prostate cancer or predicting the relative prospects of a particular outcome of prostate cancer predisposition by obtaining a sample containing only cells from tissues or a sample of urine, semen, blood, or lymphatic circulation, and (ii) determing whether the sample contains any level of any nucleic acid of Pax 2 associated with prostate cancer. The specification teaches a method of detecting the expression, presence alone, of Pax2 mRNA in all three established prostate cancer cell lines(LNCaP, DU-145, and PC-3), in 3 out of 5 channel prostate cancer TURP tumour samples, and in 10 out of the 15 radical prostatectomy specimens from

patients with prostate cancer all following RNA extractions, RT-PCR and Southern hybridizations. The specification also teaches the inability to detect Pax 2 mRNA expression in benign prostatic hyperplasia(BPH) samples in all five samples tested. The specification then teaches that Pax 2 expression is linked with prostatic cancer but not with benign prostatic hyperplasia. The specification has not established a clear correlation between the susceptibility of a human patient to prostate cancer or predicting the relative prospects of a particular outcome of prostate cancer predisposition by obtaining a sample containing only cells from tissues or a sample of urine, semen, blood, or lymphatic circulation, and (ii) determing whether the sample contains any level of any nucleic acid of Pax 2 associated with prostate cancerG/G genotype and the occurrence of bipolar II depressive disorder. More specifically, the specification does not teach the detection of Pax 2 mRNA expression in a patient without cancer, solely as a means to determine how susceptible a patient is to prostate cancer. The specification omits any teaching concerning the detection of Pax 2 mRNA as a predisposing factor to the patient's future development of prostate cancer. The specification itself on Page 27 asserts that "Pax 2 expression may be detected in prostate cancer tissue, particularly from invasive prostate cancer, but may not be detected in normal prostate tissue". Furthermore, the specification omits any teaching of the detection method's ability to determine particular outcomes of prostate cancer. On page 62, five prostate samples were obtained from patients known to have metastatic prostate cancer, but the results of this study were the same as those done with non-metastatic prostate samples thereby not teaching any difference in one particular outcome at least being metastaic potential, for example, through the detection of Pax 2 mRNA. Furthermore, the specification teaches only the detection of mRNA expression, presence or absence, through RT-PCR followed

by gel electrophoresis and Southern blot detection methods. The specification has not taught a variant grade or level at which the Pax 2 mRNA is detected only that it "is" or "is not". The specification has not taught that Pax 2 DNA or any other Pax 2 nucleic acid besides Pax 2 mRNA is present in prostate cancer cell lines and tissue samples. The specification has further omitted teachings of Pax 2 mRNA being found in any cell from a prostate tissue or in urine, semen, blood, or lymphatic circulation, only in tissue samples from the prostate and from well known prostate cell lines. The specification does not teach a method broadly drawn to determining the susceptibility of a human patient to prostate cancer or predicting the relative prospects of a particular outcome of prostate cancer predisposition by obtaining a sample containing only cells from tissues or a sample of urine, semen, blood, or lymphatic circulation, and (ii) determing whether the sample contains any level of any nucleic acid of Pax 2 associated with prostate.

As stated in *Vaek* (20 USPQ2d 1438), the specification must teach those of skill in the art how to make and how to use the invention as *broadly* as it is claimed" (emphasis added). The amount of guidance needed to enable the invention is related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher* 427 F. 2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Predictability or lack thereof in the art refers to the ability of one of skill in the art to extrapolate the disclosed or known results to the invention that is claimed. If one of skill in the art can readily anticipate the effect of a change in the subject matter to which the claimed invention is directed, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change in the subject matter to which the claimed invention is directed, then there is unpredictability in the art. With respect to the present

invention, one cannot readily anticipate a method broadly drawn to determining the susceptibility of a human patient to prostate cancer or predicting the relative prospects of a particular outcome of prostate cancer predisposition by obtaining a sample containing only cells from tissues or a sample of urine, semen, blood, or lymphatic circulation, and (ii) determing whether the sample contains any level of any nucleic acid of Pax 2 associated with prostate. One cannot anticipate whether or not a subject will get prostate cancer if the Pax 2 mRNA cannot be detected in the normal prostate(Specification Pg27). Also, it is highly unpredictable to assume that all nucleic acids besides just mRNA can be found in any cell from tissues or in a sample of urine, semen, blood, or lymphatic circulation in addition to the samples from prostate tissue that have been taught in the specification. In the absence of specific guidance as to how to identify both the susceptibility and the ability to predict the outcome of prostate cancer through the detection of all nucleic acids in cells from tissues or a sample of urine, semen, blood, or lymphatic circulation, it would require undue experimentation, if not impossible to detect a Pax 2 DNA in a blood sample that may not even be present in a normal prostate sample. The unpredictability in the art is emphasized by the teachings in the Applicant's specification regarding the lack of Pax 2 expression in normal prostate tissue with regard to the ability of the method to determine a patient's susceptibility to prostate cancer. The prior art corroborates the unpredictability in the art with respect the the teaching of a method that can predict the relative prospects of a particular outcome of prostate cancer concerning chromosome 10 alterations in Gray et al. It should be noted that the art teaches that there is no clear correlation of loss of chromosome 10q with tumor stage or grade, (Gray et al. Cancer Research 55, 1995) which adds further unpredictability about this inventions ability of predicting outcomes by detection of Pax2(located also on 10q). With

respect to the present invention, one cannot readily anticipate the method's ability to determine susceptibility and predict outcomes of prostate cancer thorugh the detection of any nucleic acid in samples other than tissue samples from the prostate. Such random trial by error experimentation is considered to be undue and in view of the high level of unpredictability in the art and the lack of guidance provided in the specification, undue experimentation would be required for one of skill in the art to practice the invention as it is broadly claimed.

The specification provides no guidance as to how to predictably identify additional samples wherein the claimed methods will result in the detection of Pax 2 mRNA in a certain level in any sample other than tissue that would be correlated with prostate cancer. Furthermore, the specification fails to teach how these detected nucleic acids actually result in any of the claimed method's ability to predict susceptibility or disease outcomes. Consequently, the resulting levels of Pax 2 will be variable and unpredictable, if not prophetic making the comparison of levels, not even defined in the specification, of nucleic acids require undue experimentation. The ability to establish a correlation between the aforementioned methods and any level detected from any nucleic acid in a method broadly drawn to determining the susceptibility of a human patient to prostate cancer or predicting the relative prospects of a particular outcome of prostate cancer predisposition by obtaining a sample containing only cells from tissues or a sample of urine, semen, blood, or lymphatic circulation, and (ii) determing whether the sample contains any level of any nucleic acid of Pax 2 associated with prostate is highly unpredictable and can only be determined through extensive, random, trial and error experimentation. Therefore, neither the specification nor the art provides the guidance necessary to practice the method as claimed. In view of the high level of unpredictability in the art and the

lack of guidance provided in the specification, undue experimentation would be required for one of skill in the art to practice the invention as it is broadly claimed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-9 and 15-16 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 1-9 and 15-16 are indefinite over the recitation of "a level". This phrase makes the claims unclear because the specification does not define what amount is encompassed by "a level". There is no fixed definition in the art for what constitutes "a level". It is unclear, eg. whether the term refers to an exact amount that will provide guidance as to which specific class/grade of tumor to which a prostate sample belongs or rather if it is just "a level" as apposed to no level ie no expression being detected. The claims should be amended to clarify to what specific amount "a level" refers.

Any inquiry concerning this communication or earlier communication from the examiner should be directed to Sally Sakelaris whose telephone number is (703) 306-0284. The examiner can normally be reached on Monday-Thursday from 7:30AM-5:00PM and Friday from 1:00PM-5:00PM.

If attempts to reach the examiner are unsuccessful, the primary examiner in charge of the prosecution of this case, Carla Myers, can be reached at (703)308-2199. If attempts to reach the examiners are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)308-1119. The fax number for the Technology Center is (703)305-3014 or (703)305-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to Chantae Dessau whose telephone number is (703)605-1237.

Sally Sakelaris

6/30/2003

CARLA J. MYERS
PRIMARY EXAMINER